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Psychoactive Prescribing for Older People - What difference does 15 years make?

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Key Points:

- 1) This study examines community dispensed prescriptions from a representative sample of an entire geographical population, and reports a significant increase in psychoactive prescribing comparing 1995 to 2010.
- 2) The variation of different individual drug classes and combinations of medications over this period can be explained by the availability of new psychoactive drugs, safety concerns, and economic factors.
- 3) Reviewing changes in psychoactive prescribing practice in the community over time can help clinicians reflect upon the current and previous exposure to psychoactive medications that older people have had, and provide a platform to assess why these changes have arisen.

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Abstract

Objective: The objective of the study was to review prescribing of psychoactive medications (drugs affecting the central nervous system) for older residents within Tayside.

Methods: The analysis used community-prescribing data in 1995 and 2010 for all older residents in Tayside. For each psychoactive drug class, the name of the most recently prescribed drug and date prescribed were extracted. The relative risk (RR) and 95% confidence intervals for patients receiving psychoactive medication in 2010 was compared to patients in 1995. Psychoactive prescribing was analyzed by year, age, gender, and deprivation classification. The chi-squared test was used to calculate statistical significance.

Results: Total psychoactive prescribing in the over 65s has increased comparing 1995 to 2010. Antidepressant [RR=2.5 (2.41-2.59) p-value=<0.0001], and opioid analgesia [RR=1.21 (1.19-1.24) p-value=<0.0001] prescriptions increased between 1995 and 2010. Hypnotics/anxiolytic [RR=0.69 (0.66-0.71) p-value=<0.0001], and antipsychotic [RR=0.83 (0.77-0.88) p-value=<0.0001] prescriptions decreased between 1995 and 2010. An increase in psychoactive prescribing is particularly marked in lower socioeconomic quintiles. Patients in quintile 1 (least affluent) had RR=1.25 (1.20-1.29) [p-value=<0.0001] of being prescribed one to two psychoactive medications, and RR=1.81 (1.56-2.10) [p-value=<0.0001] of being prescribed three or more psychoactive medications in 2010 compared to 1995. The RRs for quintile 5 (most affluent) were RR=1.14 (1.1-1.19) [p-value=<0.0001] and RR=1.2 (1.01-1.42)

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[p-value=<0.0001] for one to two and three or more medications respectively.

Conclusion: Psychoactive medication prescribing has increased comparing 1995 to 2010, with increases disproportionately affecting patients in lower socioeconomic groups. The availability of new psychoactive drugs, safety concerns, and economic factors may explain these increases.

Introduction

We are living in an increasingly ageing society, with a recent report by the United Nations stating that in 2050 for every one child, there will be four people aged 80 years or over (United Nations, 2009). The potential implications of an ageing society are wide ranging, with healthcare services being particularly affected. Older people (>65 years) may have different healthcare needs, are more likely to have co-morbid diseases, are commonly prescribed multiple drugs, and are at a greater risk of both adverse drug reactions (ADRs) and ADR related hospital admissions (Mizokami et al 2012; Ruiter et al, 2012). Importantly, older people are often prescribed medications with psychoactive properties, agents that affect mood, perception, cognition, behavior or consciousness as a result of changes in the functioning of the central nervous system (Thronson & Pagalilauan, 2014). These medications are known to have a considerable side-effect profile in older patients (Guthrie et al, 2010). The properties of psychoactive medications may be intentional to manage particular patient symptoms or a side-effect of a medication prescribed for another reason. Research assessing psychoactive drug prescribing in older patients showed that patients over 65 are not uncommonly prescribed antidepressants (10.8%), hypnotic/anxiolytics (7.5%) and antipsychotic medications (1%) (Guthrie et al, 2010). Furthermore, it is common for patients to be prescribed more than one agent with psychoactive properties (Guthrie et al, 2010; Hughes et al, 2012). However, studies of temporal changes in psychoactive prescribing are limited in number and have tended to focus only on individual drug classes.

Information gained from assessing trends in the prescribing of a single psychoactive

drug is valuable. However, assessing changes in multiple psychoactive drug groups over a period of time will provide more information about how these drugs as a whole are utilized by healthcare professionals to treat conditions, how broader changes in clinical practice may influence the prescription rates of certain agents and how different groups of patients are affected by these wider changes in clinical practice. Furthermore, reviewing the prescriptions of multiple psychoactive drugs will assist further research into the potential pharmacological burden that patients prescribed several psychoactive drugs may experience. Indeed, psychoactive drug burden is becoming an important area in clinical research, for clinical areas such as falls (Pratt et al, 2014) and cognition (Narayan et al, 2013).

This study reports a descriptive epidemiology study of dispensed psychoactive medications in a representative population of older people resident in the Tayside region of Scotland, United Kingdom. The aim of the study was to review prescribing trends of psychoactive medications for older patients within Tayside in 1995 and 2010 providing information both on patients taking single psychoactive medications and patients on multiple psychoactive agents. In addition to reviewing the overall changes in psychoactive prescribing, we wished to compare how different demographic variables impacted the overall changes in prescribing between 1995 and 2010.

Methods

The analysis uses community dispensed prescribing data for all residents of the Tayside region of Scotland held by the University of Dundee Health Informatics Centre (HIC). Data were extracted from 315 General Practices participating in the Scottish Program for Improving Clinical Effectiveness – Primary Care (SPICE-PC), a program that covers 31% of all Scottish general practices (Elder et al, 2007).

Data were fully anonymised by HIC, and all analysis was compliant with HIC Standard Operating Procedures that have been approved by the NHS East of Scotland Research Ethics Service and the NHS Tayside Caldicott Guardian. Ethical review of this specific project was therefore not required. Analysis was carried out in SPSS v18.0 (SPSS Inc, 2009). Data were extracted for people aged 65 and over on two dates – 31st March 1995 and 31st March 2010. After reviewing the datasets, 165 duplicate records were removed (ie- identical patient records appearing twice in either the 1995 or 2010 dataset). Demographic data extracted included age, gender and postcode- assigned deprivation score (Scottish Index of Multiple Deprivation (SIMD) Quintiles), and was linked to dispensed prescribing data. The SIMD is based upon information from the major population surveys in Scotland - the Scottish Household Survey, the Scottish Health Survey, the Scottish Crime and Justice Survey and the Annual Population Survey (Scottish Index of Multiple Deprivation, 2012). It provides a method of comparing the differences between the most deprived areas and the rest of the population in Scotland, in areas such as the labor market; education; health; crime; transport; and perceptions of neighborhood and local public services (Scottish Index of Multiple Deprivation, 2012).

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For each individual, community dispensed prescriptions for psychoactive drugs were extracted. Psychoactive medications were defined after consulting the British National Formulary (BNF) published in 2012 (BNF, 2012). Thus, drugs defined as psychoactive included hypnotics (defined as drugs in BNF chapter 4.1.1), anxiolytics (BNF chapter 4.1.2), drugs used in psychosis (BNF chapter 4.2), antidepressants (BNF chapter 4.3), and opioid analgesics (BNF chapter 4.7). All of these drug classes have been associated with clinically important side-effects for older people as a direct result of their actions on the central nervous system (Fastbom & Schmidt, 2010; Milos et al, 2014; Moore & O'Keeffe, 1999).

For each drug class, the name of the most recently prescribed drug and the date prescribed were extracted, and a drug was defined as 'currently prescribed' if it had been prescribed in the 84 days before the 31st March 1995 or the 31st March 2010. Therefore, only drugs dispensed in the last 84 days in both data-sets were deemed a current prescription and used in the analysis. The proportion of people aged 65 and over prescribed each drug class was calculated for patients in 1995 and patients in 2010. The eleven combinations of medications using antipsychotics, hypnotic/anxiolytics, antidepressants and opioid analgesia were then analyzed. In addition, to establish baseline characteristics of total prescribing for each individual (i.e. not only psychoactive prescribing), community dispensed prescription for all drugs were recorded as a total number (with no information about drug name and dose).

The relative risk (RR) and 95% confidence intervals for patients receiving

psychoactive medication in 2010 was compared to patients in 1995. A psychoactive drug count was calculated by adding up prescribed medications in all of the psychoactive drug classes. Hypnotic and anxiolytic medications were able to be separated in this analysis, giving a psychoactive drug count ranging from 0 to 5. Psychoactive prescribing trends were analysed by year, age, gender, and deprivation classification. The chi-squared test was used to determine whether observed changes were significantly different from chance.

Results

Patient Characteristics in 1995 and 2010

There were a total of 67,608 patients aged 65 and over who were registered with a Tayside practice in 1995 and 73,465 patients in 2010. Table 1 summarizes the main patient characteristics in the 1995 and 2010 datasets.

There was a considerable increase in the net number of patients over the age of 65 living in Tayside between 1995 and 2010, with the median age increasing by one year to 74. There were additional differences in the gender ratios and deprivation quintiles comparing 1995 to 2010. Comparing 1995 and 2010 the number of women over 65 decreased by 3.4% relative to the male population [p-value= <0.0001] and there was a decrease in the number of patients in the higher three deprivation quintiles, leading to over 50% of the population being in the two lower deprivation quintiles in 2010 [p-value=<0.0001]. There was also a considerable increase in the number of total medications (i.e. all types of medications not just psychoactive medications) that patients were prescribed. There was a 24.5% increase in the total

number of patients being prescribed five or more drugs, with the number of patients being prescribed ten or more medications almost trebling between 1995 and 2010 [p-value=<0.0001]. Importantly, there was almost a 50% reduction in the proportion of patients prescribed no medications [p-value=<0.0001].

Insertion of Table 1.

Prescribing Trends by Age Band and Gender

Table 2 presents the proportions of patients prescribed any psychoactive medications in 1995 and 2010 by age and gender. Patients in all age groups were relatively more likely to be prescribed one or more psychoactive agents in 2010 compared to 1995. At both time points there was a steady increase in the proportion of patients that were prescribed a psychoactive medication as they aged, with the proportions for all five-age brackets being greater in 2010.

Insertion of Table 2

Women are prescribed more psychoactive medication than men in both 1995 and 2010, although the overall relative percentage increase in prescribing comparing 1995 to 2010 was higher in the male group. In 1995 the RR of a female being prescribed any psychoactive medication compared to a male was 1.69 [95% CI 1.65-1.74 p-value=<0.0001] with this decreasing to 1.49 [95% CI 1.49-1.52 p-value=<0.0001] in 2010. In particular, women were more likely to be prescribed three or more psychoactive medications in both 1995 and 2010 compared to men, with a RR of 2.97 [95% CI 2.59-3.41 p-value=<0.0001] in 1995 and RR of 2.15 [95% CI 1.95 – 2.36 p-value=<0.0001] in 2010 .

Prescribing Trends by Socioeconomic Status

Overall there has been an increase in psychoactive medication prescribing across all socioeconomic groups between 1995 and 2010. However, changes in psychoactive prescribing have not been the same across the socioeconomic spectrum.

Despite all groups seeing an increase in RR of being prescribed psychoactive medications, patients in higher socioeconomic groups have seen smaller increases of risk of being prescribed psychoactive medications. Patients in quintile 1 (least affluent) had a 1.25 [95% CI 1.20-1.29 p-value=<0.0001] RR of being prescribed one or two psychoactive medications and a 1.81 [95% CI 1.56 – 2.10 p-value=<0.0001] RR of being prescribed 3 or more psychoactive medications in 2010 compared to 1995. The RRs for patients in quintile 3 was 1.14 [95% CI 1.09-1.18 p-value=<0.0001] and 1.61 [95% CI 1.36-1.9 p-value=<0.0001] for being prescribed one or two psychoactive medications and three or more psychoactive medications respectively. The RR for patients in quintile 5 were 1.14 [95% CI 1.1- 1.19 p-value=<0.0001] and 1.2 [95% CI 1.01-1.42 p-value=<0.0001] for being prescribed one or two psychoactive medications and three or more psychoactive medications respectively.

Trends in Psychoactive Prescribing

Table 3 notes the prevalence of patients prescribed one or more of the psychoactive drugs assessed in this study [antidepressants, drugs used in psychoses, opioid analgesia and hypnotics/anxiolytics] in 1995 and 2010. RR ratios, two-tailed p-valued and 95% confidence intervals are also noted in the table.

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The prescription of two medications decreased between 1995 and 2010, hypnotic/anxiolytic medications and drugs used for psychoses. Furthermore, the RR of being prescribed no psychoactive medications decreased over the same period. However, the RR of being prescribed antidepressants and opioid analgesia was significantly higher in 2010 compared to 1995.

Eleven combinations of psychoactive medications were then reviewed. The prescription of three psychoactive medications combinations decreased comparing 1995 to 2010: hypnotic/anxiolytic & opioid analgesia, hypnotic/anxiolytic & drugs used for psychoses, and drugs used for psychoses & opioid analgesia. The other eight combinations increased in frequency in 2010 compared to 1995. Two combinations increased considerably, antidepressants & opioid analgesia and hypnotic/anxiolytic & opioid analgesia & antidepressants.

Insertion of Table 3.

Table 4 shows the results of a psychoactive drug count and includes all 5 psychoactive groups (separating hypnotic and anxiolytic medications). Therefore, this drug count ranges from zero (patient is not prescribed any drugs from the five CNS active drug classes) to five (patient is prescribed drugs from all of the five CNS active drug classes). Patients have an increased RR of being prescribed between one and five psychoactive medications in 2010 compared to 1995.

Insertion of Table 4

Discussion

Key Findings

Between 1995 and 2010, there was an increase in the number of people living in Tayside (Scotland) over the age of 65, reflecting the change in the United Kingdom as a whole (Rutherford, 2012). In addition, there was a significant increase in social deprivation according to SMID social deprivation scoring quintiles.

The study has reported that people over 65 in Tayside, were more likely to receive medications of all forms in 2010 compared to 1995. Indeed, between 1995 and 2010 the total number of all drugs dispensed increased from a median of 3 in 1995 to 5 in 2010, alongside a statistically significant 23.6% increase in older people taking 5 or more medications. Importantly, this study reports that psychoactive medication prescribing has increased in 2010 compared to 1995. However, these increases have varied depending upon psychoactive drug class, with prescriptions of antidepressant and opioid analgesia increasing and prescriptions of antipsychotics and hypnotic/anxiolytics reducing. Patients are also more likely to be prescribed multiple psychoactive medications in 2010 compared to 1995. Furthermore, the relative increases in psychoactive prescribing in 1995 compared to 2010 have been significantly greater in lower socioeconomic groups.

The prescription of psychoactive drugs to patients over 65 years old has recently become an area of intense interest both medically and politically (Banerjee, 2009). Clearly, prescribing psychoactive medications to this patient group is often clinically

appropriate and safe, but the risks that these drugs may pose to older people are increasingly recognized. One recent study reported that despite increasing evidence of adverse outcomes, the proportion of older people prescribed anticholinergic medications and the proportion with a high anticholinergic exposure has increased between 1995 and 2010 (Sumakadas et al, 2013). In 2009 a report reviewing antipsychotic use in dementia patients estimated that current antipsychotic prescribing patterns were likely to cause over 1,600 cerebrovascular events and up to 1,800 avoidable patient deaths (Banerjee, 2009). Numerous other studies have linked psychoactive medications to adverse outcomes including reduced cognition, reduced mobility and adverse drug reactions (Banerjee, 2009; Boudreau et al, 2009; Gray et al, 2002; Guthrie et al, 2011; Lowry et al, 2011; Sumakadas et al, 2013).

Assessing changes in psychoactive prescribing practice in the community over time can help clinicians reflect upon the current and previous exposure to psychoactive medications that older people have had, and provide a platform to assess why these changes have arisen. Such work can help direct efforts to develop and improve current clinical practice. A strength of this particular study is that it examines community dispensed use for a representative sample of an entire geographical population (Elder et al, 2007; Sumakadas et al, 2013).

Prescribing Trends by Age Band and Gender

This study reports that the total number of all drugs dispensed increased when comparing 2010 prescriptions to 1995 prescriptions. In relation to psychoactive medications there was an increase in RR of receiving one or more psychoactive

medications for all five age bands between 1995 and 2010.

As patients age they are more likely to be prescribed medications of all forms (Mizokami et al, 2012; Ruiter et al, 2012). This has become more pronounced over the last 15 years due to new medications in conditions commonly affecting older people, such as cardiovascular disease, osteoporosis and diabetes mellitus (Wise, 2013). Recently, there has been a focus upon promoting rational prescribing and reviewing repeat prescriptions of older people because of the increase in polypharmacy (The Model of Care Polypharmacy Working Group, 2012; O'Mahony et al, 2010; Wise, 2013). Initiatives that aim to optimize prescribing for older people through service developments within primary care (The Model of Care Polypharmacy Working Group, 2012), are particularly important as it has been reported that physicians can feel that solutions to inappropriate prescribing of medication, in particular psychoactive prescribing, is beyond the scope of the individual physician (Damestoy, Collin & Lalande, 1999). In the past, successful approaches to optimizing prescribing for older people have usually been either educational or administrative, and a combination of these approaches is recommended (Mort & Aparasu, 2002). For example, in America the Omnibus Budget Reconciliation Act of 1987 served as an impetus for clinical review and changed practice style for prescribing in nursing homes (Lantz, Giambanco & Buchalter, 1996) and was noted to reduce antipsychotic prescribing in nursing homes by linking Medicare reimbursement to appropriate prescribing (Gurvich & Cunningham, 2000; Lantz, Giambanco & Buchalter, 1996; Mort & Aparasu, 2002). In the UK, linking prescribing reviews to the Quality Outcomes Framework (QOF) which awards family doctors points based upon their

management of patients, may be able to achieve similar results by allowing primary care physicians to be paid for reviewing older patients prescriptions and making appropriate adjustments. In the future, making exception reporting easier (ie: allowing a doctor to receive a QOF point despite not prescribing a statin in a frail and multi-morbid older man with high cholesterol) may allow family practitioners to provide rational prescribing to older people both in terms of psychoactive prescribing and more broadly.

In both years, 1995 and 2010, women were more likely to be prescribed psychoactive medications compared to men. This may relate to the fact that women are more likely to have been treated for a mental health problem than men (29% compared to 17%) (National Statistics, 2003). It is postulated that this is because women report symptoms of the most common mental health disorders more readily to primary care physicians (Gurvich & Cunningham, 2000; National Institute for Clinical Excellence, 2009). Furthermore, men are more likely to develop conditions where psychoactive prescribing is not generally indicated long-term, such as alcohol and substance misuse (National Statistics, 2003). Psychoactive prescribing increased for both genders between 1995 and 2010, which may relate to the management of depression and anxiety disorders with the newer antidepressants not available in 1995, alongside the increased use of opioid prescribing for pain syndromes.

Prescribing Trends by Socioeconomic Status

This study reports that older patients in lower economic quintiles were more likely to be prescribed psychoactive medications in both 1995 and 2010. In 2010 over 50%

of the population were placed in the two lower deprivation quintiles following complex social and economic changes to the population. Based upon analysis of previous economic experiences, a nation's economic health is intricately linked with its mental and physical health (Cooper, 2011; The Black Report, 1980). Financial crises with their associated rising unemployment, social inequality and social insecurity have been linked with higher suicide rates and less clear relationships with increases in prevalence of psychiatric illnesses, alcohol-related disorders and drug use (Cooper, 2011). Indeed, English data collected between 2008 - 2011 following the recession, reported increases of more than 40% in the number of people seeking treatment for mental health disorders, and an increase in the number of people diagnosed with depression by 11.5% (SSentif Online, 2013). Therefore, higher levels of social deprivation in 2010 may partially explain higher rates of psychoactive prescribing in 2010 compared to 1995. This increase may reflect higher rates of both mental and physical ill health in patients in the lower economic quintiles.

Trends in Psychoactive Prescribing

The prescription of hypnotic/anxiolytic medications and drugs used for psychoses decreased between 1995 and 2010. The authors postulate that the reduction in drugs used for psychoses was mainly due to the large-scale reduction in the prescription of thioridazine, rather than a reduction of all agents in this drug group. Thioridazine was an atypical antipsychotic that was used in the 1990s as an anxiolytic and sedative (at lower doses). The drug was withdrawn from the market worldwide in 2005 following concerns about high rates of cardiotoxicity and of fatal dysrhythmias when compared to other antipsychotics (Purhonen et al, 2012; Reilly

et al, 2000). Indeed in contrast to our finding of a reduction in antipsychotic prescribing, there have been numerous concerns about the over-use of antipsychotic medications in older patients with dementia to manage behavioral and psychological symptoms of dementia, despite the literature being skeptical of their efficacy (Banerjee, 2009; Declercq et al, 2013; Gustafsson et al, 2013; Guthrie et al, 2010). Furthermore, a study looking at the prescribing pattern of psychoactive drugs in nursing home residents with dementia, concluded that of all psychoactive drugs antipsychotics were the most commonly prescribed drug class (Wetzels et al, 2011).

The significant reduction in the prescription of hypnotic and anxiolytic agents appears to reflect concerns about drug dependence, tolerance and efficacy alongside the occurrence of significant side-effects in older people. Indeed, there is clear evidence that benzodiazepines and other sedative-hypnotic medications significantly increase the risk of falls and hip fractures in older people (American Geriatric Society Choosing Wisely Working Group, 2013). Furthermore, these medications may lead to cognitive problems in the over 65s, with a meta-analysis of randomised controlled trials enrolling older adults reporting that memory problems, disorientation, and confusion are more common with benzodiazepines and newer non-benzodiazepine hypnotics than placebo (Glass et al, 2005). Finally, there is evidence that newer antidepressants may be able to manage patients with anxiety more safely (Lieberman, 2003) and the non-drug options for managing anxiety (National Institute for Clinical Excellence, 2009) and insomnia (Lamberg, 2008) now have good evidence basis.

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The prescription of antidepressants and opioid analgesia increased between 1995 and 2010. Antidepressant medications have evolved since 1995 with dual-acting (norepinephrine and serotonin) antidepressants such as venlafaxine, duloxetine and mirtazapine now available (National Institute for Clinical Excellence, 2009). In addition, over the last decade there has been research looking into how these agents may be used to treat other conditions including anxiety and neuropathic pain (National Institute for Clinical Excellence, 2009). Finally, compared to 1995 the majority of patients with depression have their condition and prescriptions handled entirely in the community by primary care physicians (National Institute for Clinical Excellence, 2009; van Weel, van Weel-Baumgarten & van Rijswijk, 2009).

The increase in opioid analgesia prescriptions appear to relate primarily to efforts over the last decade to improve the management of pain in older patients, which has historically been under-treated (Hughes, 2012; National Institute for Clinical Excellence, 2012). The National Institute of Clinical Excellence (NICE) have reported that strong opioids are the principal treatments for pain related to advanced and progressive disease, and their use has increased significantly in the primary care setting in recent years (National Institute for Clinical Excellence, 2012). Indeed, there have been numerous guidelines that have reviewed the use of opioid analgesia in older people (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain, 2012; National Institute for Clinical Excellence, 2012). These guidelines have suggested that these medications are both effective and safe in older people when prescribing cautions are implemented by prescribers (e.g. starting initial titration at no more than 50% of the suggested initial dose for adults

and lengthening the time interval between dose increases). However, in the US there does remain concern that the prescription of opioid analgesia in non-cancer patients may be excessive and other therapeutic options under-used (Daubresse et al, 2013).

The changes in drug combinations between 1995 and 2010 appear to reflect changes in individual psychoactive medications during this period.

Limitations

This research paper has several limitations that should be considered each in turn. Firstly, this paper reports a patient being prescribed a psychoactive medication based upon community prescription data at two specific time-points, once in 1995 and once in 2010. Therefore, the data obtained does not allow us to fully ascertain the changes in prescribing practice that have arisen over this period of time, merely to compare these two time points. However, such work can be used to provide a platform for a discussion in relation to psychoactive prescribing. Secondly, due to the nature of the dataset, we were unable to analyze high-risk patient groups in relation to psychoactive prescribing, such as those residing in nursing homes, care homes, sheltered housing or receiving significant community support. This will be the focus of future clinical research, as assessing psychoactive prescribing in these groups and comparing them to community-dwelling adults is of great importance. Thirdly, no information on the dose of the drug or whether this was an acute, delayed or repeat prescription was available. Finally, the data only reflects community-prescribing practice, and changes in the same period in secondary care are out-with the scope of

this report. However, the paper does highlight several potential areas for further work such as hospital prescribing practice, focused research on the relationship between economic status and psychoactive prescribing, and psychoactive prescribing in the oldest old.

Conclusion

Psychoactive medication prescribing has increased in 2010 compared to 1995, with these increases disproportionately affecting patients in lower socioeconomic groups. These changes can be explained by the development and changing safety profiles of medications, an ageing multimorbid population, a focus upon prescribing in older patients and socioeconomic factors. Reviewing changes in prescribing practice in the community over time provides a useful platform for discussion.

Conflicts of Interest

Competing Interest Declaration

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that the study received no external funding and the authors have no financial conflicts of interest to report.

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Declaration of Original Publication

This manuscript contains original unpublished work and is not being submitted for publication elsewhere.

Ethics

Data used in this research study were fully anonymised by University of Dundee Health Informatics Centre (HIC), and all analysis was compliant with HIC Standard Operating Procedures that have been approved by the NHS East of Scotland Research Ethics Service and the NHS Tayside Caldicott Guardian. Therefore, no ethical approval was required for this study.

Authorship

All authors meet the requirements to be named as authors by the International Journal of Geriatric Psychiatry. Each of the authors meet all of the following criteria:

1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; 3) final approval of the version to be published.

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Table 1. Description of Patient Characteristics

1995 Tayside Dataset [n= 67,608]	2010 Dataset [n=73,465]	Two-Tailed P-Value
Median Age : 73 years [IQR- (25)- 69 years; (75)- 80 years]	Median Age : 74 years [IQR- (25)- 69 years; (75)- 80 years]	<0.0001
60.1% Female (n=40632) 39.9% Male (n=26976)	56.7% Female (n=41655) 43.3% Male (n=31810)	<0.0001 <0.0001
Number of all drugs dispensed in last 84 days Median number of dispensed drugs:- 3 drugs [IQR- (25)- 0 drugs; (75)- 5 drugs] 23.8% (n=16091) are taking 0 medications 46.7% (n=31573) are taking 1-4 medications 29.5% (n=19944) are taking 5+ medications 5.8% (n=3921) of those taking 5+ medications are taking ≥ 10	Number of all drugs dispensed in last 84 days Median number of dispensed drugs:- 5 drugs [IQR- (25)- 2 drugs; (75)- 8 drugs] 12.1% (n=8889) are taking 0 medications 33.9% (n=24904) are taking 1-4 medications 54% (n=39671) are taking ≥ 5 medications 16.9% (n=12415) of those taking ≥ 5 medications are taking ≥ 10	<0.0001 <0.0001 <0.0001 <0.0001
Scottish Deprivation Quintiles* Q1 – 17.7% (n=11967) Q2 – 17.7% (n=11967) Q3 – 17.9% (n=12101) Q4 – 29.9% (n=20215) Q5 – 16.8% (n=11358)	Scottish Deprivation Quintiles* Q1 – 12.6% (n=9257) Q2 – 14.5% (n=10652) Q3 – 17.5% (n=12856) Q4 – 33.7% (n=24758) Q5 – 21.7% (n=15942)	<0.0001 <0.0001 0.1021 <0.0001 <0.0001

* Scottish Deprivation Quintiles- socioeconomic deprivation based on the Scottish Index of Multiple score for the patients postcode of residence. Quintile 1 is most deprived and Quintile 5 is most affluent

Table 2. Number of Psychoactive Medications Prescribed in 1995 & 2010

	1995 % prescribed any psychoactive	2010 % prescribed any psychoactive (number)	RR (95% CI) 2010 compared to 1995	Two-Tailed P- Value
Men	21.1 (n= 5,695)	27.4 (n= 8,708)	1.3 (1.26 – 1.34)	<0.0001
Women	35.7 (n= 14,524)	40.9 (n= 17,046)	1.14 (1.12 – 1.16)	<0.0001
65-69 years old	23.4 (n= 4,763)	29.9 (n= 6,137)	1.28 (1.23 – 1.32)	<0.0001
70-74 years old	27.3 (n= 4,998)	32.9 (n= 5,941)	1.20 (1.17 – 1.24)	<0.0001
75-79 years old	32.2 (n= 3,896)	36.2 (n= 5,413)	1.12 (1.09 – 1.16)	<0.0001
80-84 years old	37.4 (n= 3,531)	39.6 (n= 4,268)	1.06 (1.03 – 1.1)	0.0009
≥ 85 years old	40.6 (n= 3,031)	43.6 (n= 3,995)	1.07 (1.04 – 1.11)	<0.0001

Table 3. Prevalence of psychoactive drug prescribing in people 65 and over in 1995 and 2010.

	Number of patients (%) in the 1995 cohort. n = 67,608	Number of patients (%) in 2010 cohort. n = 73,465	RR (95% CI) 2010 compared to 1995	Two-tailed P-Value
<i>Currently Prescribed</i>				
None of the 4 drug classes	48,553 (71.8)	49,797 (67.8)	0.94 (0.94 - 0.95)	<0.0001
Any Hypnotic/Anxiolytic	8,270 (12.2)	5,956 (8.1)	0.69 (0.66 - 0.71)	<0.0001
Any Antidepressant	3,666 (5.4)	9,938 (13.5)	2.5 (2.41 - 2.59)	<0.0001
Any Drugs used in Psychoses	1,763 (2.6)	1,582 (2.2)	0.83 (0.77 - 0.88)	<0.0001
Any Opioid Analgesia	11,254 (16.6)	14,812 (20.2)	1.21 (1.19 - 1.24)	<0.0001
<i>Currently Prescribed Combinations</i>				
Hypnotic/Anxiolytic and Antidepressant	1,264 (1.9)	2,229 (3.0)	1.62 (1.52 - 1.74)	<0.0001
Hypnotic/Anxiolytic and Drugs used in Psychoses	576 (0.9)	544 (0.7)	0.87 (0.77 - 0.98)	0.021
Hypnotic/Anxiolytic and Opioid Analgesia	2,841 (4.2)	2,286 (3.1)	0.74 (0.70 - 0.78)	<0.0001
Antidepressant and Drugs used in Psychoses	482 (0.7)	734 (0.9)	1.40 (1.25 - 1.57)	<0.0001
Drugs used in Psychoses and Opioid Analgesia	393 (0.6)	407 (0.6)	0.96 (0.84 - 1.1)	0.5206
Opioid Analgesia and Antidepressant	1,246 (1.8)	4,000 (5.4)	2.95 (2.77 - 3.15)	<0.0001
Hypnotic/Anxiolytic and Drugs used in Psychoses and Antidepressant	184 (0.3)	294 (0.4)	1.47 (1.22 - 1.78)	<0.0001
Hypnotic/Anxiolytic and Drugs used in Psychoses and Opioid Analgesia	143 (0.2)	164 (0.2)	1.06 (0.84 - 1.33)	0.679
Hypnotic/Anxiolytic and Antidepressant and Opioid Analgesia	508 (0.8)	998 (1.4)	1.81 (1.62 - 2.01)	<0.0001
Antidepressant and Drugs used in Psychoses and Opioid Analgesia	126 (0.2)	216 (0.3)	1.58 (1.26 - 1.98)	<0.0001
All 4 drug classes	57 (<0.1)	92 (0.1)	1.49 (1.06 - 2.1)	0.0226

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Table 4. Number of Psychoactive Medications Prescribed in 1995 & 2010

		Number of Psychoactive Medications [Drug Count]					
		0	1	2	3	4	5
1995	Patient Number (%)	47389 (70.1)	14197 (21.0)	4662 (6.9)	1124 (1.7)	218 (0.3)	18 (<0.1)
2010	Patient Number (%)	47711 (64.9)	17217 (23.4)	6307 (8.6)	1792 (2.4)	386 (0.5)	52 (0.1)
	RR 2010 compared to 1995	0.93	1.12	1.25	1.47	1.63	2.71
	95% CI	(0.92 - 0.93)	(1.09 - 1.14)	(1.20 - 1.29)	(1.36 - 1.58)	(1.38 - 1.93)	(1.51 - 4.88)
	Two-Tailed P-Value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0004